

<b>FORM PTO-1449</b> <b>INFORMATION DISCLOSURE STATEMENT</b>				<b>SERIAL NO.</b>		10/595,932	
				<b>FILING DATE</b>		May 19, 2006	
				<b>APPLICANT</b>		Mercep et al.	
				<b>GROUP</b>		1617	
				<b>EXAMINER</b>		K.D. Carter	
				<b>ATTORNEY DOCKET NO.</b>		PLP527USw	
<b>U.S. PATENT DOCUMENTS</b>							
<b>Examiner Initials</b>		<b>Patent Number</b>	<b>Issue Date</b>	<b>Name</b>	<b>Class</b>	<b>Subclass</b>	<b>Filing Date If Appropriate</b>
	1	3,773,940	Nov. 20, 1973	Schindler et al.			
	2	3,781,294	Dec. 25, 1973	Lombardino			
	3	3,859,439	Jan. 7, 1975	Blattner et al.			
	4	3,894,032	July 8, 1975	Remy			
	5	3,974,285	Aug. 10, 1976	Remy			
	6	4,044,143	Aug. 23, 1977	Remy			
	7	4,112,110	Sept. 15, 1978	Blattner			
	8	4,267,184	May 12, 1981	Cherkofsky et al.			
	9	4,267,190	May 12, 1981	Cherkofsky et al.			
	10	4,271,179	June 2, 1981	van der Burg			
	11	5,917,057	June 29, 1999	Hamer et al.			
	12	2003/0153750	Aug. 14, 2003	Mladen et al.			
	13	2005/0148578	July 7, 2005	Mercep et al.			
Continue on page _____							
<b>FOREIGN PATENT DOCUMENTS</b>							
		<b>Document Number</b>	<b>Publication Date</b>	<b>Country</b>	<b>Class</b>	<b>Subclass</b>	<b>Translation Yes   No</b>
	14	EP 0125484	Nov. 21, 1984	EUROPE			
	15	EP 0357126	Mar. 7, 1990	EUROPE			
	16	EP 0372445	June 13, 1990	EUROPE			
	17	WO 91/18885	Dec. 12, 1991	WIPO			
	18	WO 98/54186	Dec. 3 1998	WIPO			
	19	WO 99/00355	Jan. 7, 1999	WIPO			X Abstract
	20	WO 03/084961	Oct. 16, 2003	WIPO			
	21	WO 03/097649	Nov. 27, 2003	WIPO			
	22	WO 03/099823	Dec. 4, 2003	WIPO			
	23	HR 20000310	Feb. 28, 2002	CROATIA			X
	24	HR 20020453	May 23, 2002	CROATIA			X
Continue on page _____							
<b>OTHER DOCUMENTS (Including Author, Title, Journal-Date, Page Number, Etc.)</b>							
	25	Ackermann L., Harvima I.T. "Mast cells of psoriatic and atopic dermatitis skin are positive for TNF- $\alpha$ and their degranulation is associated with expression of ICAM-1 in the epidermis." Arch. Dermatol. Res. 1998, 290:353-359.					
	26	Aderka, D. "Role of tumor necrosis factor in the pathogenesis of intravascular coagulopathy of sepsis: potential new therapeutic implications." Isr. J. Med. Sci., 1991, 27:52-60.					
	27	Arrieta O, et al. "Protective effect of pentoxifylline plus thalidomide against septic shock in mice." Int. J. Exp. Pathol. 1999, 80(1):11-16.					
	28	Badger A.M. et al. "Beneficial effects of the phosphodiesterase inhibitors BRL 61063, pentoxifylline, and rolipram in a murine model of endotoxin shock." Circ. Shock 1994 44(4):188-195.					
	29	Badger et al. "Pharmacological profile of SB 203580, a selective inhibitor of cytokine suppressive binding protein/p38 kinase, in animal models of arthritis, bone resorption, endotoxin shock and immune function." J. Pharmac. Env. Therap., 1996, 279(3):1453-1461.					
	30	Becker et al. "Photochemistry of the Anthracene Chromophore: Novel Isomerization of 1-(9-Anthryl)-2-Benzoethylenes." Tetrahedron Lett., 1985. 26(12):1589-1592.					
	31	Bennett et al. "Reaction of 5-acetyl-10, didehydro-5H-dibenz[b,f] azepine with pyrrole, N-methylpyrrole, imadazole and n-methylimidazole: cycloaddition versus Michael addition." J. Heterocycl. Chem., 1994, 31:293-296.					

32	Bissonnette E. Y. et al. "Inhibition of tumour necrosis factor-alpha (TNF-alpha) release from mast cells by the anti-inflammatory drugs, sodium cromoglycate and nedocromil sodium." Clin. Exp. Immunol. 1995, 102:78-84.
33	Bresnihan. "Treatment with recombinant human interleukin-1 receptor antagonist (rhIL-1ra) in rheumatoid arthritis (RA); results of randomized double-blind, placebo-controlled multicenter trial." Arthrit. Rheum., 1996, 39:73.
34	Cagniant. C.R. Hebd. Sceances Acad. Sci., 1976, 283:683-686
35	Carswell et al. "An endotoxin-induced serum factor that causes necrosis of tumors." Proc. Natl. Acad. Sci. U.S.A., 1975, 72:3666-3670.
36	Chapman P.T. et al. "Endothelial activation in monosodium urate monohydrate crystal-induced inflammation: in vitro and in vivo studies on the roles of tumor necrosis factor alpha and interleukin-1." Arthritis Rheum., 1997, 40:955-965.
37	Cheung A. T. et al. "An in vivo model for elucidation of the mechanism of tumor necrosis factor-alpha (TNF-alpha)-induced insulin resistance: evidence for differential regulation of insulin signaling by TNF-alpha." Endocrinology, 1998, 139:4928-4935.
38	Collier et al. "The abdominal constriction response and its suppression by analgesic drugs in the mouse." Br. J. Pharmac. Chemother., 1968, 32:295-310
39	Corral L., et al. "Differential Cytokine Modulation and T Cell Activation by Two Distinct Classes of Thalidomide Analogues That are Potent Inhibitors of TNF- $\alpha$ ." The Journal of Immunology 1999, 163:380-386.
40	Dibbs Z, et al. "Cytokines in heart failure:pathogenetic mechanisms and potential treatment." Proc. Assoc. Am. Physicians, 1999, 111:423-428.
41	Di Francia M. et al. "Tumor necrosis factor-alpha levels and weight loss in chronic obstructive pulmonary disease." AM. J. Respir. Crit. Care Med. 1994, 150:1453-1455.
42	Dinarello. "An update on human interleukin-1: From molecular biology to clinical relevance." J. Clinical Immunology, 1985, 5:287.
43	Dinarello. "Interleukin-1." Rev. Infect. Disease, 1984, 6(1):51-95.
44	Duong D.J. et al. "American experience with lowdose thalidomide therapy for severe cutaneous lupus erythematosus." Arch. Dermatol. 1999 135 (9):1079-1087.
45	Egido J. et al. "Role of tumor necrosis factor-alpha in the pathogenesis of glomerular diseases." Kidney Int. Suppl. 1993, 39:59-64.
46	Elliott et al. "Randomised double-blind comparison of chimeric monoclonal antibody to tumor necrosis factor alpha (cA2) versus placebo in rheumatoid arthritis." The Lancet, 1994, 344:1105-1110.
47	M. Feldman et al. "Role of Cytokines in Rheumatoid Arthritis." Annu. Rev. Immunol. 1996 14:397-440.
48	Fukawa et al. "A method for evaluating analgesic agents in rats." J. Pharmacol. Meth., 1980, 4:251-259.
49	Funke et al. "Physico-chemical properties and stability of trans-5-chloro-2-methyl-2,3,3a,12b-tetrahydro-1-dibenz[2,3:6,7]oxepino[4,5-c]pyrrolidine Maleate. Arzeim-Forsch., 1190, 40:536-539.
50	Gauldie J. et al. "Cytokines and pulmonary fibrosis." Thorax, 1993, 48:931-935.
51	Georgopoulos et al. "Transmembrane TNF is sufficient to induce localized tissue toxicity and chronic inflammatory arthritis in transgenic mice." J. Inflamm., 1996, 46:86-97.
52	Gruschwitz, M., et al. "In situ Expression and Serum Levels of Tumor Necrosis Factor- $\alpha$ Receptors in Patients with Early Stages of Systemic Sclerosis." Journal Rheumatology 1997; 24:1936-43.
53	Heilig, B. et al. "Elevated TNF Receptor Plasma Concentrations in Patients with Rheumatoid Arthritis." Clinical Investigation 1992; 70:22-27.
54	Heilig B et al. "[Expression of TNF receptors in rheumatoid arthritis and ankylosing spondylitis]." [Article in German]. Z Rheumatol. 1993 Nov-Dec; 52(6):383-9.
55	Hotamisligil G.S., Spiegelman B.M. "Tumor necrosis factor alpha: a key component of the obesity-diabetes link." Diabetes, 1994, 43:1271-1278.
56	Huff, J.R. "HIV Protease: A novel chemotherapeutic target for AIDS." Journal of Medicinal Chemistry, 34(8), pgs. 2305-2314.
57	Iyer and Gopalachari. "Studies in Potential Antifertility Agents: Part VII - Sythesis of Dialkylaminoethyl Derivatives of 2,4,5Triphenylpyrroles & 2,4,5Triphenylfurans." Indian J. Chem., 1973, 11:1260-1262.
58	Jones et al. "Antiestrogens. 2. Structure-activity studies in a series of 3-aroyle-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]-phenyl]methanone hydrochloride (LY156758), a remarkably effective estrogen antagonist with only minimal intrinsic estrogenicity." J. Med. Chem., 1984, 27:1057-1066.
59	Kapadia S. et al. "The role of cytokines in the failing human heart." Cardiol. Clin., 1998, 16:645-656.
60	Keffer, et al. "Transgenic mice expressing human tumour necrosis factor: a predictive genetic model of arthritis." EMBO J., 1991, 10:4025-4031.
61	King, F.D. "Bioisosteres, Conformational Restriction, and Pro-Drugs – Case History: An Example of a Conformational Restriction Approach." Med. Chem.: Principle and Practice (1994) p. 206-208.
62	Kluth D.C., Rees A.J. "Inhibiting inflammatory cytokines." Semin. Nephrol. 1996, 16:576-582.
63	Kopicova et al. "Potential Tetracyclic Neuroleptics: 12-(4-methylpiperazino)benzo[b]naphtho[2,3-f]theipin and its 12,13-dihydro Derivative." Collect. Czech. Chem. Commun., 1975.40:1960-1965.

64	Kopicova and Protiva. "Synthesis of 7-(4-methylpiperazino)-7,8-dihydrobenzo[b]naphtho[2,1-f]thiepin and of Related Compunds." Collect. Czech. Chem. Commun., 1974, 39:3147-3152.
65	Krakauer T, Stiles BG. "Pentoxifylline inhibits superantigen-induced toxic shock and cytokine release." Clin Diagn Lab Immunol. 1999 Jul;6(4):594-8.
66	Liedtke W. "Effective Treatment of Models of Multiple Sclerosis by Matrix Metalloproteinase Inhibitors." An. of Neurology, 1998, Vol. 44; 35-46.
67	Liu J.Y. et al. "TNF-alpha receptor knockout mice are protected from the fibroproliferative effects of inhaled asbestos fibers." Am. J. Pathol., 1998, 153:1839-1847.
68	Maini R.N, Taylor P.C. "Anti-Cytokine Therapy for Rheumatoid Arthritis." Annu. Rev. Med. 2000 51:207-229.
69	Martel-Pelletier J., Alaaeddine N. Pelletier JP. "Cytokines and their role in the pathophysiology of osteoarthritis." Front Biosci, 1999 4:D694-703.
70	Matsukawa A, et al. "Analysis of the Cytokine Network Among Tumor Necrosis Factor $\alpha$ , Interleukin-1 $\beta$ , Interleukin-8 and Interleukin-I Receptor Antagonist in Monosodium Urate Crystal-Induced Rabbit Arthritis." Lab Invest 1998; 78:559-569.
71	Mattioli and Ghia. "Omega-dialkylaminoalkyl ethers of phenyl-(5-substituted 1-phenyl-1H-pyrazol-4-yl)methanols with analgesic and anti-inflammatory activity." J. Heterocyclic Chem., 1997, 34:963-968.
72	McHugh et al. "Preparation of 8H-Furo[3,4-d]dibenz[b,f]azepine. A Novel Heterocyclic Ring System." J. Heterocycl. Chem., 1990, 27:1839-42.
73	Mori et al. "Photochemical reactions of anthracene-naphtalene bichromophoric systems linked by a three-carbon chain." J. Chem. Soc., Perkin Trans. 2, 1996, 1:113-119.
74	Mori et al. "Attenuation of collagen-induced arthritis in 55-kDa TNF receptor type 1 (TNFR1)-IgG1-treated and TNFR1-deficient mice." J. Immunol., 1996, 157:3178-3182.
75	Noguchi, M., et al. "Secretion Imbalance between Tumor Necrosis Factor and its inhibitor in inflammatory bowel disease." Gut 1998, 43:203-209.
76	Novacek et al. "Reaction of 8-chloro-10-phenylhydrazono-10, 11-dihydro-dibenzo[b,f]thiepine with aromatic aldehydes." Collection Czechoslov. Chem. Commun., 1976, Vol. 41, 785-787.
77	Nyiondi-Bonguen et al. "[4+2] - Cycloadditions of 3-Amino-4-imino-4H-thieno[3,4-c][l]benzopyran with some Selected Dienophiles." J. Chem Soc., Perkin Trans. 1, 1994, 15:2191-2195.
78	Odeh M. "Role of Cytokines in Rheumatoid Arthritis." Drugs News Perspect. 11(6) 1998, 331-341.
79	Oliver S., et al. "The Effect of Thalidomide and 2 Analogs on Collagen Induced Arthritis." Journal of Rheumatology 1998; 25:964-9.
80	Olivera et al. "Dibenzoxepino '4,5-d pyrazoles: a facile approach via the Ullman-ether reaction." Tetrahedron Letters, 2000, 41(22):4353-4360.
81	Peleman R.A., Kips J.C., Pauwels R.A. "Therapeutic activities of theophylline in chronic obstructive pulmonary disease." Clin. Exp. Allergy 1998 28 Suppl 1. 3:53-56.
82	Pfeffer et al. "Mice deficient for the 55kd tumor necrosis factor receptor are resistant to endotoxic shock, yet succumb to L. monocytogenes infection." Cell, 1993, 73:457-467.
83	Piguet P.F. et al. "Expression and localization of tumor necrosis factor-alpha and its mRNA in idiopathic pulmonary fibrosis." Am. J. Pathol. 1993, 143:651-655.
84	Piguet P.F., Vesin C. "Treatment by human recombinant soluble TNF receptor of pulmonary fibrosis induced by bleomycin or silica in mice." Eur. Respir. J., 1994, 7:515-518.
85	Reimund J. "In vitro effects of oxpentifylline on Inflammatory Cytokine Release in Patients with Inflammatory Bowel Disease." Gut 1997, 40:475-480.
86	Ross S., et al. "Suppression of TNF $\alpha$ Expression, Inhibition of TH1 Activity and Amelioration of Collagen-Induced Arthritis by Rolipram." Journal of Immunology, 1997, 159:6253-6259.
87	Rutgeerts P. et al. "Efficacy and Safety of Retreatment with Anti-Tumor Necrosis Factor Antibody (Infliximab) to Maintain Remission in Crohn's Disease." Gastroenterology., 1999, 117:761-769.
88	Sandborn W. and Hanauer S. "Antitumor Necrosis Factor Therapy for Inflammatory Bowel Disease; A review of Agents, Pharmacology, Clinical Results and Safety." Inflammatory Bowel Diseases 1999, 5(2):119-133.
89	Saricaoglu H. et al. "Prevention of nickel-induced allergic contact reactions with pentoxifylline." Contact Dermatis 1998, 39(5):244-247.
90	Sasayama S. et al. "New insights into the pathophysiological role for cytokines in heart failure." Cardiovasc Res. 1999, 42:557-564.
91	Schmidt H. et al. "Thalidomide inhibits TNF response and increases survival following endotoxin injection in rats." J. Surg. Res. 1996 63(1):143-146.
92	Schulz et al. "Synthese von 1,3a,3,12b-tetrahydro-dibenzo[b,f]-pyrazolo[3,4-d]azepin-Derivaten." Z. Chem. 1988, 28:181-182.
93	Schweizer et al. "Combined automated writhing/motility test for testing analgesics." Agents and Actions, 1988, 23:29-31.
94	Shire, MG and Muller GW. "TNF- $\alpha$ inhibitors and rheumatoid arthritis." Exp. Opin. Ther. Patents. 1998 8(5): 531-544.
95	Stirling D. I. Semin. "Thalidomide and its impact in dermatology." Cutan. Med. Surg. 1998 17(4):231-242.

96	Sykes A.P. et al. "The effect of an inhibitor of matrix metalloproteinases on colonic inflammation in a Erinitrobenzenesulphonic acid rat model of inflammatory bowel disease." Aliment Pharmacol Ther. 1999, 13:1535-1542.
97	Taylor R. Multiple Sclerosis: A Rehabilitative Approach, 1998, 9, 3, 525-536. "Immunologic Aspects of Multiple Sclerosis."
98	Tochtermann et al. Ein neuer Zugang zu chiralen Tribenzocycloheptarien-(Tribenzo-[a.c.e]cyclohepten-) und Tribenzo[b.d.flthiepin-S.S-dioxid-Derivaten." . Chem. Ber., 1968, 101:3122-3137.
99	Tomizawa S. et al. "TNF inhibitory activity in the urine of chronic renal failure patients with glomerulonephritis." Nephron. 1993, 63:111-112.
100	Tsuji et al. "Studies on Anti-Inflammatory Agents. VI. Synthesis and Pharmacological Properties of 2,3-Diarylthiophenes." Chem. Pharm. Bull., 1998, 46(2):279-286.
101	Ueda et al. "The Synthesis of 10-(4-Methylpiperazino)dibenzo[b,flthiepin and Related Compunds. Neurotrpic and Psychotropic Agents." Chem. Pharm. Bull., 1975, 23(10):2223-2231.
102	Van Assche and Rutgeerts. "Anti-TNF agents in Chrohn's disease." Exp. Opin. Invest. Drugs, 2000, 9:103-111.
103	van den Berg, W.B. "Anti-Cytokine Therapy in Chronic Destructive Arthritis." Arthritis Res 2001, 3:18-26.
104	Vippagunta, S.R. et al. "Crystalline solids." Advanced Drug Delivery Reviews, 2001, 48(1):3-26.
105	Westacott C.I. et al. "Tumor necrosis factor alpha can contribute to focal loss of cartilage in osteoarthritis." Osteoarthritis Cartilage 2000 8(3):213-221.
106	Postmarketing Adverse Event Data for TNF-alpha Antagonists (October 23, 2001). Stephen A. Paget, MD < <a href="http://rheumatology.hss.edu/phys/specialreports/pagettnf.asp">http://rheumatology.hss.edu/phys/specialreports/pagettnf.asp</a> >
107	Green (Using TNF alpha technology to treat rheumatoid arthritis) Article (July/August 2004). < <a href="http://rheumatology.hss.edu/phys/specialreports/pagettnf.asp">http://rheumatology.hss.edu/phys/specialreports/pagettnf.asp</a> >
108	Centocor products (08/11/2004) < <a href="http://www.centocor.com/cgi-bin/site/products/prod_remicade.cgi">http://www.centocor.com/cgi-bin/site/products/prod_remicade.cgi</a> is cited for the statement that>
109	"News & Notices: <a href="http://www.psoriasis.org/enbrel.approval.jan02.htm">http://www.psoriasis.org/enbrel.approval.jan02.htm</a> (7/30/2002).
Continue on page _____	
EXAMINER	DATE CONSIDERED
EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.	